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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,835	12/24/2001	Yunik Chang	HME/7679.012	9339
29085	7590	09/28/2004	EXAMINER	
HOWARD EISENBERG, ESQ. 2206 APPLEWOOD COURT PERKASIE, PA 18944			MAIER, LEIGH C	
			ART UNIT	PAPER NUMBER
			1623	
DATE MAILED: 09/28/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

<p align="center"><b>Office Action Summary</b></p>	<p><b>Application No.</b></p> <p>10/033,835</p>	<p><b>Applicant(s)</b></p> <p>CHANG ET AL.</p>	
	<p><b>Examiner</b></p> <p>Leigh C. Maier</p>	<p><b>Art Unit</b></p> <p>1623</p>	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 26 July 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 24-86 and 88-91 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 24-51, 56-78, 80-86 and 88-91 is/are rejected.
- 7) ☒ Claim(s) 52-55 and 79 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| <p>1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)</p> <p>2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)</p> <p>3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br/> Paper No(s)/Mail Date _____.</p> | <p>4) <input type="checkbox"/> Interview Summary (PTO-413)<br/> Paper No(s)/Mail Date. _____.</p> <p>5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)</p> <p>6) <input type="checkbox"/> Other: _____.</p> |
|---|---|

## **DETAILED ACTION**

### ***Status of the Claims***

Claims 24, 25, 45, 47, 52, 78, 82-84, 86, and 89 have been amended. Claim 87 has been canceled. Newly submitted claim 91 has been added. Claims 24-86 and 88-91 are pending. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Any objection or rejection not expressly repeated has been withdrawn.

Applicant is reminded of the rules regarding amendments to claims. Claim 45 is identified as "amended," but this amended claim has no markings to indicate changes. It is further noted that the correct status identifier is "currently amended" as was used in the other amended claims.

### ***Allowable Subject Matter***

Claims 52-55 and 79 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 89-91 would be allowable with the requirement for MTZ in claim 89.

Applicant argues cogently that there is some evidence of synergy in the composition comprising MTZ,  $\beta$ -cyclodextrin (BCD), and niacinamide (Nd). However, the evidence presented is not commensurate with the scope of the invention as claimed. It appears that the basis for the unexpected results is the added NCA allows for a solution comprising BCD at or above the limit of solubility, that is, at least 0.5% w/w, that is stable at 5°C. Therefore, the claims

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incorporating these limitations are allowable. It is noted that claim 79 does not have the stability requirement, but it does recite both the BCD and Nd concentrations wherein synergy is demonstrated and the stability at 5°C is an inherent property.

***Claim Rejections - 35 U.S.C. § 102***

Claims 82-84, 89, and 90 are rejected under 35 U.S.C. 102(b) as being anticipated by STRUENGMANN et al (WO 99/09988). This reference was cited and made of record in the first Office action, June 19, 2003.

STRUENGMANN discloses a composition comprising BCD and Nd. The composition is dissolved in aqueous buffer. The reference is silent regarding stability at 5°C. Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980).

***Claim Rejections - 35 U.S.C. § 103***

Claims 24, 27-29, 31, 32, 40, 41, 43-51, 56-58, 63, 65-68, 71-74, 76-78, 80-82, 85, and 86 are rejected under 35 U.S.C. 103(a) as being obvious over KATA et al (Acta Pharm. Hung., 1984) and CHIEN et al (US 4,032,645).

Applicant's arguments filed July 26, 2004 have been fully considered but they are not persuasive.

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Applicant first submits that the examiner's statement regarding claims 74 and 76-79.

Applicant states that this invention "provides the ability to solubilize more MTZ in aqueous fluid than would ordinarily be possible due to the limited aqueous solubility of BCD." However, the only step in both instances is combining the three components. The examiner maintains that they are essentially the same invention.

Applicant argues that the percentages for the components disclosed by KATA are not credible because the reference reports a BCD concentration that is at odds with those reported in other references submitted by Applicant. However, it is noted that all of these reference report the maximum solubility of uncomplexed BCD. One of these references, REDENTI et al (J. Pharm. Sci., 2000 – made of record on the attached PTO-892) teaches that solubility of CDs is enhanced by complexation. See page 2, the paragraph bridging the two columns. Even if it is the case that the solutions disclosed are not stable at 5°C, these claims have no limitations regarding stability and BCD concentration. Claims 45 and 82 require the former but not the latter. Claim 78 requires the latter but not the former.

Applicant further notes that with BCD only, the maximum stable concentration of MTZ is 0.8% w/w. However, the combination of references teaches the use of BCD in combination with other solubilizing agents, such as Nd or Nn. The synergy demonstrated at the limit of BCD solubility is noted above, but there is no evidence of this at lower concentrations.

Claims 24, 26-51, 56-68, 70-74, 76-78, 80-82, 85, 86, and 88 are rejected under 35 U.S.C. 103(a) as being obvious over KATA et al (Acta Pharm. Hung., 1984) and CHIEN et al (US 4,032,645) in view of CZERNIELEWSKI (US 5,849,776).

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Applicant's arguments filed July 26, 2004 have been fully considered but they are not persuasive.

Applicant argues that CZERNIELEWSKI does not disclose whether the disclosed compositions are suspension or solution gels. Applicant further contends that the reference "does not disclose how a solution composition having a MTZ concentration higher than 0.75% may be made" and that the artisan "may not make a solution composition of MTZ higher than 0.75% by following the disclosure of CZERNIELEWSKI.

It would be within the scope of the artisan to select known composition type known to have utility. It is noted that in discussing compositions having utility for topical administration, the reference lists ". . . solutions, gels, sprays, lotions or suspensions." One of ordinary skill would surmise that either type of gel would have utility.

The reference may not *exemplify* compositions having a MTZ concentration higher than 0.75% but clearly teaches their utility. While the examiner does not concede that one of ordinary skill would not be able to prepare *any* solution having a MTZ concentration higher than 0.75%, Applicant is correct to the extent that one of ordinary skill could not prepare the *instant* solution by reliance on CZERNIELEWSKI alone. The examiner maintains that the instant solution is obvious over the combination of references of record.

Claim 24, 25, 27-29, 31, 32, 40, 41, 43-51, 56-58, 63, 65-69, 71-74, 76-78, 80-82, 85, and 86 is rejected under 35 U.S.C. 103(a) as being obvious over KATA et al (Acta Pharm. Hung., 1984) and CHIEN et al (US 4,032,645) in view of LOFTSSON (US 5,324,718).

Applicant's arguments filed July 26, 2004 have been fully considered but they are not persuasive. Applicant presents no additional arguments not addressed above.

Claims 82-84 and 88-91 are rejected under 35 U.S.C. 103(a) as being obvious over STRUENGMANN et al (WO 99/09988).

STRUENGMANN teaches the meloxicam compositions comprising BCD and Nd, as set forth above. The reference further teaches that gels comprising meloxicam have ophthalmic utility. See page 2, third full paragraph.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare the compositions exemplified in the reference and modify them by adding a gelling agent to prepare a gel for the art-disclosed utility of ophthalmic administration.

Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

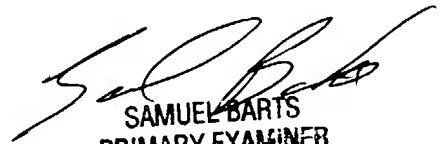
*Examiner's hours, phone & fax numbers*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Wednesday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (571) 272-0661, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 872-9306.

Visit the U.S. PTO's site on the World Wide Web at <http://www.uspto.gov>. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

Leigh C. Maier  
Patent Examiner  
September 27, 2004

  
SAMUEL BARTS  
PRIMARY EXAMINER  
GROUP 1600